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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
08/836,576	09/09/1997	JEAN HAENSLER	0725.0100000	6479

20306 7590 03/26/2003

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EXAMINER	
LUCAS, ZACHARIAH	
ART UNIT	**PAPER NUMBER**
1648	

DATE MAILED: 03/26/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	08/836,576	HAENSLER ET AL.	
	Examiner	Art Unit	
	Zachariah Lucas	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 June 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *28, 30-37, 61-69, and 75-88* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *28,30-37,61-69 and 75-88* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status of the Claims

1. Claims 25-88 were rejected in the action mailed on October 25, 2000 (the prior action). Claims 25-27, 29, 38-60, and 70-74 were cancelled, and claims 28, 30, 33, 36, 37, 62, and 75 were amended in the response filed June 21, 2001 (Amend. E). Currently, Claims 28, 30-37, 61-69, and 75-88 are pending and under consideration in the application.

2. The Art Unit location of your application, and the examiner to whom the case has been docketed in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Examiner Zachariah Lucas in Art Unit 1648.

Information Disclosure Statement

3. The information disclosure filed on June 21, 2001 contains reference to patent 5,053,585, issued to Allison et al. However, the patent filed with the IDS was numbered 4,053,585. This patent otherwise fit the fit the description in the IDS. Patent 5,053,585 does not deal with relevant subject matter, or meet the remainder of the document description in the IDS. Thus, the reference in the IDS (the 5,053,585 patent) has not been considered, but the 4,053,585 patent has been considered and is, for convenience, made of record in the notice of references cited attached to this action.

Specification

4. **(Prior Objections-Withdrawn)** In the prior action, the specification was objected for lacking a heading to the Brief Description of the Drawings section, and for the inclusion of Tables 1 and 2 in the body of the specification, rather than as figures. These objections are withdrawn in view of the amendments made in Amend. E.

5. **(New Objection)** The disclosure is objected to because of the following informalities: In the chart on page 15 of the application, the first identified composition appears to include negative 15 μg of HA, and 0 (mg) of DC-Chol. It is unclear what is meant by "- 15 μg," but it is assumed, from the text of the specification on line 6 of the same page, that the applicant intended to describe a composition comprising 15 μg of HA.

Appropriate correction is required.

Claim Objections

6. **(New Objection- Necessitated By Amendment)** Claims 28, 30-37, 62-69, and 75-88 are objected to because of the following informalities: Claim 30 was amended in Amend. E to read on a vaccine composition to read on a vaccine composition comprising 3-E-(N-(N-N'-dimethylaminoethane)carbamoyl) cholesterol. It appears that in the making of the Amendment, the composition described above was inserted in the place of the compound 3β-(N-(N', N'-

dimethylaminoethane)carbamoyl) cholesterol (or DC-Chol). The same seems to apply to claims 36 and 37. The remaining claims are objected to a dependant on these claims.. Appropriate correction is required.

7. **(New Objection- Necessitated By Amendment)** Claim 31 is objected to because it is not further limiting of the claim from which it depends. For the purposes of this objection, it is being assumed that the compound of claim 30 is supposed to be 3β-(N-(N', N'-dimethylaminoethane)carbamoyl) cholesterol. Claim 31 reads the vaccine composition of claim 30, wherein the adjuvant is 3β-(N-(N', N'-dimethylaminoethane)carbamoyl) cholesterol. Claim 31 is therefore requiring that the composition of claim 30 comprise a compound already required by the independent claim. Thus, the dependant claim is not further limiting of the claim from which it depends, and is therefore improper under 37 CFR § 1.75(c).
and ((dimethylaminoethane or polyethylenamine) with (cholesterol) or dc-chol)

8. **(New Objection- Necessitated By Amendment)** Claim 32 is objected to because it is not further limiting of the claim from which it depends. This claim reads on the vaccine composition of claim 30, wherein the adjuvant is 3β-(n-(polyethylenamine)carbomoyl) cholesterol. However, claim 30 specifies that the adjuvant of the vaccine described in that claim is 3β-(N-(N', N'-dimethylaminoethane)carbamoyl) cholesterol. Thus, claim 32 is not further limiting of claim 30, but is attempting to recharacterize the vaccine described in that claim. Thus, the dependant claim is not further limiting of the claim from which it depends, and is therefore improper under 37 CFR § 1.75(c).

Claim Rejections - 35 USC § 112

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

10. (Prior Rejection- Withdrawn in part, and restated) Claims 47 and 59 were rejected for indefiniteness in the prior action. As these claims have been cancelled for the application, the rejection is withdrawn as to these claims. However, the same grounds for rejection also applies to claim 34. Thus, claim 34 is rejected for the reasons of record regarding cancelled claims 47 and 59.

11. **(New Rejection- Necessitated By Amendment)** Claim 28 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This claim reads on the composition of claim 30, wherein the antigen is influenza antigen. It is unclear if a composition with particular influenza antigen is being claimed, or if any influenza antigen may be used. It is suggested that the applicant insert the word "an" before influenza antigen.

12. **(New Rejection- Necessitated By Amendment)** Each of claims 31, 32, 61, 80, 81, 82, 84, 85, and 86 recite the limitation "said amphipathic adjuvant." There is insufficient antecedent basis for this limitation in the claim. The claims from which these claims depend do not

introduce "an amphipathic adjuvant." Because these claims are reciting a limitation that has been cancelled from the pending independent claims, it is unclear what the subject matter of these claims is.

13. **(New Rejection- Necessitated By Amendment)** Claim 61 recites the limitation "the vaccine composition of claim 50" in the preamble. There is insufficient antecedent basis for this limitation in the claim. This claim depends from a claim that has been cancelled from the application. As the claim depends from a claim not in the application, it is unclear what vaccine is being further identified. The claim is therefore indefinite.

14. **(New Rejection- Necessitated By Amendment)** Claim 75, dependant claims 76-86, and 88, are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 75 describes a method of inducing an immune response in a mammal comprising administering to the mammal at least one antigen, and the vaccine composition of claim 30. Claim 30 reads on a vaccine composition comprising at least one antigen and a cholesterol derivative. Thus, claim 75 appears to require the presence of two antigens, one alone and one in the vaccine combination of claim 75. It is unclear whether the antigen described in claim 75 is intended to be a separate antigen administered to the animal separately from the vaccine, if the second antigen is intended to be combined with the vaccine composition, or if the inclusion of the second at least one antigen was unintentional.

15. **(New Rejection- Necessitated By Amendment)** Claim 83 recites the limitation "wherein said lipophilic group is a cholesterol derivative." There is insufficient antecedent basis for this limitation in the claim. As the claims from which this claim depends (directly or indirectly) do not introduce a lipophilic group, or indicate what this group is a part of, the claim is indefinite. Thus, claim 83, its dependant claims, claims 84-86, are rejected as indefinite.

16. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

17. **(New Rejection)** Claims 32, 84, and 86, are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a vaccine comprising DC-Chol as an adjuvant, does not reasonably provide enablement for vaccine compositions comprising any of the other compounds identified in claims 32, 84, or 86 as adjuvants. The specification has not provided adequate description to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. For the purposes of this rejection, the claims are being interpreted as a vaccine composition, or method of using such, comprising an antigen and 3β-(n-(polyethylenamine)carbomoyl) cholesterol or one of 4 other compounds including DC-Chol. This claim is rejected because the applicant has provided adequate support that the claimed compounds other than DC-Chol would be useful as adjuvants.

According to the applicant, the art teaches away from such a use of these compounds. See, Amend. E, pages 5 and 6. The applicant also refers to art teaching that that there a number

of factors involved in the adjuvanticity of a compound, and that there no formula that one in the art could use to determine if a particular liposome would have value as an adjuvant. Page 5. Thus, the applicant has demonstrated that there is great deal of uncertainty in the art regarding what lipsomal compositions may and may not be used as adjuvants. Further, given the fact that the art teaches away from the use of cholesterol derivatives adjuvants, this uncertainty would appear to be even greater with respect to the inventions claimed in the instant application. Thus, the art both tends to indicate that the claimed cholesterol would not be an effective adjuvant, and that one skilled in the art would not be readily able to determine if a particular composition would be effective.

The applicant has demonstrated that DC-Chol is likely to be useful as an adjuvant. The applicant has disclosed only compositions comprising DC-Chol, or DC-Chol in combination with other compounds. However, the applicant has not provided any evidence that showing that the other compounds would have adjuvant properties. Given the teachings regarding the uncertainty in the art, the disclosure of a single related embodiment is not sufficient to support claims to other potentially effective compounds. Further, while the application appears to have shown that DC-Chol may be an effective adjuvant, it does not show or describe what it is about this compound makes it an effective adjuvant. Without such a teaching, one skilled in the art would not have any guidance towards, or evidence regarding the efficacy of, the other adjuvant compounds. Thus, the applicant has not enabled the presently claimed invention.

Claim Rejections - 35 USC § 102

18. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

19. **(New Rejection)** Claims 30, 31, 34-37, 62, 64, 67, 75, and 78 are rejected under 35 U.S.C. 102(a) as being anticipated by Hiu et al, J. Liposome Res., 4(3):1075-1090 (November 1994, of record in the IDS filed on October 17, 1997). For the purposes of this rejection, these claims are being interpreted as describing a vaccine composition, and method of using it, comprising an antigen and DC-Chol. There is no limitation regarding what may constitute an antigen. Thus, this term is read as including any compound that elicits a specific immune response.

Hui teaches a genetic vaccine comprising an antigenic gene, and a liposome comprising DC-Chol and dioleoylphosphatdylethanolamine (DOPE). The reference teaches a vaccine comprising a MHC complex presenting an antigenic gene) with a DC-Chol/ DOPE liposome. The polynucleotide attached to the MHC complex is intended to raise a specific immune response against an encoded peptide. It is therefore considered to be an antigen. The DC-Chol/DOPE liposome meets the claim limitations. Thus, the reference anticipates the identified claims.

It is noted that, prior to Amend. E, the claims specified that the DC-Chol was an adjuvant. Hui does not teach the adjuvant properties of DC-Chol. However, as the compound is being used in the manner described by the applicant in a vaccine composition, the compound would have inherently been acting as an adjuvant for the vaccine. Further, claim 30 as amended

does not identify DC-Chol as an adjuvant. It merely requires a vaccine composition comprising the antigen and the compound. As such, this claim is clearly anticipated by Hui without resort to inherency.

Claim Rejections - 35 USC § 103

20. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

21. **(Prior Rejections- Withdrawn in part)** Claims 25-64, 66-78, and 80-88 were rejected in the prior action under 35 U.S.C. 103(a) as being unpatentable over either Bolcsak et al, U.S. Patent 5,100,662, in view of Gao et al., Biochem. Biophys. Res. Comm., 179: 280-285.

Claims 25-64, 66-78, and 80-88 were also rejected in the prior action under 35 U.S.C. 103(a) as being unpatentable over Popescu et al., EPA 0 356 339, in view of Epand et al., U.S. Patent 5,283,185.

Finally, claims 65 and 79 were rejected in the prior action under 35 U.S.C. 103(a) as being unpatentable over either Bolcsak et al. in view of Gao et al., or Popescu et al., in view of Epand et al., as applied to claims 25-64, 66-78, and 80-86 above, and further in view of del Prete et al., Trends in Microbiol., 2(1): 4-6.

Of the rejected claims, claims 28, 30-37, 61-69, and 76-88 remain pending in the application. The claims appear to have been amended to read on vaccine compositions comprising specific amphipathic compounds.

The applicant traverses all of these rejections on two related grounds. The applicant first argues that, in making these rejections, the examiner bridges the gap between Bolcsak and Gao, and between Popescu and Epand, by assuming that all liposomes are useful as adjuvants. The applicant argues that this is an improper assumption. The applicant then argues that there is no motivation or suggestion that DC-Chol liposomes may be used as an adjuvant. The applicant then discusses a number of references that purportedly teach away from the use of the claimed liposomes (i.e. adjuvants comprising DC-Chol). The references cited by the applicant teach away, generally, from the use of compounds with similar chemical properties as DC-Chol. See, Amend. E, page 6. Thus, given the absence of art indicating that one of ordinary skill in the art would be motivated to use, and would have a reasonable likelihood of success in the use of, a DC-Chol liposome as an adjuvant, the applicant's arguments are persuasive with regards to those claims wherein the compounds is claimed as an adjuvant.

However, while the applicant has made these arguments, the applicant has also amended the claim 30 so that it no longer requires that the compound of that claim (assumed to be DC-Chol) be an adjuvant. In view of this, the applicant's traversal is moot with regards to this claim. As the art clearly teaches that DC-Chol liposomes may be used to deliver genetic vaccines, and as no limitation is made on what comprises an antigen, the rejections of claim 30, and claims 33, 36, 37, 62-69, 75-79, 87, and 88 are maintained for the reasons of record.

Examiner's Notes

22. It was indicated above that a number of claims in the present application still include reference to a genus of vaccines comprising any amphipathic adjuvant. However, none of these claims are supported by the independent claims in the application. The claims have been rejected as improperly dependant. As none of these claims actually claim the disclosed genus, but merely refer to it, it appears that the genus is not being claimed. However, in the case that the claims are amended to read on such a genus, the examiner would like to drawn attention to a patent commonly assigned with the present application that reads on vaccine composition comprising an amphipathic compound, wherein the amphipathic compound is disclosed as an adjuvant. U.S. Patent 6,124,270, claims 11 and 15. If the claims in the present application are so amended, they will be rejected under the doctrine of obviousness type double patenting based on the claims of that patent.

Conclusion

23. No Claims are allowed.

24. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Zachariah Lucas whose telephone number is 703-308-4240. The examiner can normally be reached on Monday-Friday, 8 am to 4:30 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel can be reached on 703-308-4027. The fax phone numbers for the

organization where this application or proceeding is assigned are 703-308-4242 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Z. Lucas
Patent Examiner
March 12, 2003

JAMES HOUSEL 3/23/03
SUPERVISORY PATENT EXAMINER
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